PATENT
ATTORNEY DOCKET NO.: GENE1120-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Nolan and Filshie	Art Unit:	1636
Application No.:	09/342,024	Examiner:	G. Leffers, Jr.
Filed:	June 28, 1999		
Title:	HIGH EFFICIENCY TRANSFECTION BASED ON LOW ELECTRIC FIELD STRENGTH, LONG PULSE LENGTH		

Commissioner for Patents
Washington, D.C. 20231

DECLARATION OF DR. DIETMAR P. RABUSSAY UNDER 37 C.F.R. §1.132

Sir:

I, Dr. Dietmar P. Rabussay, do hereby declare and state that:

1. I presently hold the position of Vice President of Research and Development at Genetronics, Inc., having a place of business at 11199-A Sorrento Valley Road, San Diego, California 92121-1334

2. I hold a degree of M.Sc. (Diplomingenieur) in Chemistry granted by the Technical University of Graz, Austria in 1967 and a degree of Ph.D. (Dr, rer. Nat.) from the University of Munich, Germany, granted in 1971.

3. I have been involved in the electroporation field for over twenty years and am an author on over fifty publications, of which sixteen concern electroporation, a list of which is

attached hereto. I am also a named inventor on no less than five issued patents on electroporation technology.

4. I am familiar with the content of the above-identified application, including the methods for introducing nucleic acid into a cell of a mammalian subject *in vivo*. In addition, I have studied the Examiner's reasons in support of the rejection of claims 1-2, 4-11, 19-20 and new claims 30, 31, 34, 36, 37 and 39 of the above-identified application under 35 U.S.C. § 102(e) as allegedly being anticipated by U. S. Patent No. 5,944,710 to Dev et al. (hereinafter "the Dev patent").

5. I am also familiar with the Dev patent, particularly with disclosure contained therein pertaining to ranges of electric field strength and pulse length suitable for in vivo delivery of nucleic acid into a cell, especially cells of a mammalian subject. I disagree with the Examiner's assertion that the Dev patent discloses selecting and utilizing a *combination* of electric field strength and pulse length as claimed by the Applicants of the above-described application for *in vivo* delivery of nucleic acid into a mammalian cell. In fact, the Dev patent discloses (Dev col. 11, first full paragraph) that the preferred pulse duration range is 500 microseconds to 10 milliseconds. This is clearly below the claimed range of about 10 milliseconds to about 100 milliseconds. Thus, the Dev patent contains an express teaching of a preferred range for pulse duration that lies substantially outside the claimed range, showing that the focus of the Dev patent, and the skilled artisan's attention is directed to other than the claimed invention.

Additionally, I disagree with the Examiner's assertion that disclosure in the Dev patent of electroporation-enhanced delivery of nucleic acids intravascularly using electric fields in a broad range of at least 100-2,000V/cm (or higher), anticipates the claimed field strength range because the Dev patent also teaches that "mammalian cells typically require between 0.5 and 5.0 kV/cm" [or 500-5000 V/cm] before electroporation will occur (Dev, Col 10, lines 34-36). Thus, the Dev patent specifically discloses a field strength range appropriate for electroporation of mammalian cells that excludes most of the voltage range recited in claims 1 and 39 of the above-identified application.

Of even greater importance, there is no disclosure in the Dev patent that the *combination* of field strength of about 300-600 volts per centimeter and pulse duration of 10-100 milliseconds is to be selected and used for the case wherein nucleic acid is delivered to mammalian cells. The Dev patent discloses that the pulse length to be used for electroporation of cells can be between 100 microseconds to 100 milliseconds, preferably 500 microseconds to 10 milliseconds. Yet only a pulse length of 0.76 milliseconds was used in the Example.

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Thus, it is my observation and opinion that the Dev patent not only fails to disclose selection of the particular combination of field strength and pulse duration for electroporation enhanced *in vivo* delivery of nucleic acids to mammalian cells that is the subject matter of claims 1 and 39 of the above-described application, but in fact actually leads away from using such conditions. As a scientist who has been intimately involved in the electroporation industry for many years, it is clear that one of skill in the electroporation art would understand that Dev did not disclose each and every element of the presently claimed invention and further has not lead any artisan in the electroporation arts to be lead to use such conditions. Rather, use of the conditions claimed in the present application are new and provide an unexpected and surprising result in this art.

4. I further declare that all statements made herein of knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, or imprisonment, or both under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: December 19, 2002

Dr. Dietmar P. Rabussay

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